

CLAIMS

1. Pharmaceutical composition comprising 5 to 20% of an idazoxan salt or of idazoxan hydrate, 10 to 40% of microcrystalline cellulose, 1 to 5% of lubricant, 0.1 to 0.5% of colloidal silica and from 29.5% to 84.8% of lactose, with respect to the total mass.
2. Pharmaceutical composition according to Claim 1, in which the salt is the hydrochloride.
3. Pharmaceutical composition according to Claim 1 or 2, in which the said idazoxan is the polymorph of form I characterized by the X-ray diffraction spectrum presented in Figure 1.
4. Pharmaceutical composition according to Claim 1 or 2, in which the said idazoxan is the polymorph of form I characterized by an X-ray diffraction spectrum comprising characteristic peaks at approximately 4.0200, 6.6400, 6.9000, 7.0800, 8.0800, 9.0000, 9.9600, 9.9600, 10.8400, 11.7200, 12.1400, 12.3800, 12.9800, 13.3000, 13.5200, 14.9000, 15.0600, 15.2400 and 21.4000 degrees  $\theta$ .
5. Pharmaceutical composition according to Claim 1 or 2, in which the said idazoxan is the polymorph of form I characterized by an X-ray diffraction spectrum comprising characteristic peaks at approximately 4.0200, 6.6400, 6.9000, 7.0800, 8.0800, 9.0000, 9.9600, 9.9600, 10.8400, 11.7200, 12.1400, 12.3800, 12.9800, 13.3000, 13.5200, 14.9000, 15.0600, 15.2400 and 21.4000 degrees  $\theta$  and lacking at least one peak at approximately 4.7400, 5.7200, 8.9200, 16.8600 or 18.9000 degrees  $\theta$ .
6. Pharmaceutical composition according to Claims 3 to 5, in which the said polymorph of form I is characterized by a differential thermal analysis

thermogram exhibiting a single maximum value at approximately  $207.5 \pm 0.2$ .

7. Pharmaceutical composition according to Claim 1  
5 or 2, in which the said idazoxan is the polymorph of form III characterized by the X-ray diffraction spectrum presented in Figure 3.

8. Pharmaceutical composition according to Claim 1  
10 or 2, in which the said idazoxan is the polymorph of form III characterized by an X-ray diffraction spectrum comprising characteristic peaks at approximately  
4.0400, 4.7000, 5.7400, 6.6200, 6.9200, 7.4600, 8.0400,  
8.7800, 8.9800, 9.9800, 10.8200, 11.4600, 11.6400,  
15 12.3200, 12.9400, 13.5400, 14.2400, 15.0600, 15.6200  
and 16.8400 degrees  $\theta$ .

9. Pharmaceutical composition according to Claims 7  
and 8, in which the said polymorph of form III is  
20 characterized by a differential thermal analysis thermogram exhibiting a single maximum value at approximately  $203.8 \pm 0.5$ .

10. Pharmaceutical composition according to Claim 1  
25 or 2, in which the said idazoxan is the polymorph of form IV characterized by the X-ray diffraction spectrum presented in Figure 4.

11. Pharmaceutical composition according to Claim 1  
30 or 2, in which the said idazoxan is the polymorph of form IV characterized by an X-ray diffraction spectrum comprising characteristic peaks at approximately  
4.8000, 5.9000, 6.8400, 7.3200, 8.0800, 8.6600, 9.4600,  
9.6800, 11.1600, 11.4000, 11.9000, 12.2200, 12.6800,  
35 13.8400, 14.4200, 14.9800 and 18.1000 degrees  $\theta$ .

12. Pharmaceutical composition according to Claim 1  
or 2, in which the said idazoxan is the polymorph of form IV characterized by an X-ray diffraction spectrum

comprising characteristic peaks at approximately 4.8000, 5.9000, 6.8400, 7.3200, 8.0800, 8.6600, 9.4600, 9.6800, 11.1600, 11.4000, 11.9000, 12.2200, 12.6800, 13.8400, 14.4200, 14.9800 and 18.1000 degrees  $\theta$  and  
5 lacking at least one peak at approximately 6.6800, 13.5400, 15.6800, 16.8600 or 18.9000 degrees  $\theta$ .

13. Pharmaceutical composition according to Claims 10 to 12, in which the said polymorph of form IV is  
10 characterized by a differential thermal analysis thermogram exhibiting a single maximum value at approximately  $205.3 \pm 0.5$ .

14. Pharmaceutical composition according to Claim 1,  
15 in which the said idazoxan monohydrate is the polymorph of form V characterized by the X-ray diffraction spectrum presented in Figure 5.

15. Pharmaceutical composition according to Claim 1,  
20 in which the said idazoxan monohydrate is the polymorph of form V characterized by an X-ray diffraction spectrum comprising characteristic peaks at approximately 5.0400, 5.8400, 7.9400, 9.2800, 9.4400, 10.1200, 12.0200, 12.5600, 12.9200, 13.7400, 13.9400,  
25 14.5200, 14.8200, 15.2800, 16.2800 and 16.7400 degrees  $\theta$ .

16. Pharmaceutical composition according to Claim 1,  
in which the said idazoxan monohydrate is the polymorph  
30 of form V characterized by an X-ray diffraction spectrum comprising characteristic peaks at approximately 5.0400, 5.8400, 7.9400, 9.2800, 9.4400, 10.1200, 12.0200, 12.5600, 12.9200, 13.7400, 13.9400, 14.5200, 14.8200, 15.2800, 16.2800 and 16.7400 degrees  
35  $\theta$  and lacking at least one peak at approximately 4.7400, 6.6800, 7.5000, 8.9200, 11.5200, 14.3000, 15.6800 or 18.9000 degrees  $\theta$ .

17. Pharmaceutical composition according to Claims 14

to 16, in which the said idazoxan monohydrate polymorph of form V is characterized by a differential thermal analysis thermogram exhibiting a single maximum value at approximately  $205.6 \pm 0.4$ .

5

18. Pharmaceutical composition according to Claims 1 to 17, in which the lubricant is glyceryl behenate.

10 19. Composition according to Claims 1 to 18, which is provided in a form suitable for oral administration.

20. Tablets, comprising a pharmaceutical composition according to Claims 1 to 19.

15 21. Tablets according to Claim 20, characterized in that they have a mass of between 50 and 1 000 mg, preferably between 100 and 600 mg.

20 22. Tablets according to Claims 20 and 21, characterized in that they are provided in a leaktight packaging.

25 23. Tablets according to Claim 22, characterized in that the packaging leaktight to water vapour is composed of a tablet bottle made of polypropylene or of high-density polyethylene, of an aluminium sachet or, and preferably, of an all-aluminium blister pack.

30 24. Process for the manufacture of a tablet according to one of Claims 20 to 23, comprising a stage of direct tableting of a powder mixture.

35 25. Process for the manufacture of a tablet according to Claim 24, characterized in that the said tableting is preceded by a stage of dry granulation, for example by compacting.

26. Manufacturing process according to Claim 25, in which the active principle has a particle size,

expressed by its mean diameter, of between 50 and 250 microns.

27. Manufacturing process according to Claim 25, in  
5 which the active principle has a mean particle size preferably of between 75 and 150 microns and more particularly in the region of 100 to 125 microns.

28. Manufacturing process according to Claims 24 to  
10 27, in which the active principle has a bulk density of between 0.4 and 0.8 and preferably between 0.5 and 0.7 and more preferably still in the region of 0.6.

29. Use of a composition according to Claims 1 to 19  
15 or of a tablet according to Claims 20 to 23 as medicament intended for the preventive and/or curative treatment of a pathology selected from the group consisting of depression, Parkinson's disease and severe psychotic disorders, such as schizophrenia and  
20 schizoaffective disorders.

30. Use of a composition according to Claims 1 to 19  
or of a tablet according to Claims 20 to 23, in  
combination with an atypical antipsychotic neuroleptic  
25 exhibiting a greater antagonist affinity for the dopamine D<sub>2</sub> receptor than is its antagonist affinity for the  $\alpha_2$ -adrenoreceptor, as medicament for the preventive and/or curative treatment of severe  
psychotic disorders, such as schizophrenia and  
30 schizoaffective disorders.

31. Use according to Claim 30, characterized in that  
the said atypical neuroleptic is chosen from  
olanzapine, quetiapine, risperidone, sertindole or  
35 ziprasidone.

32. Polymeric form I of idazoxan wherein the X-Ray  
spectra comprises specific peaks at about  
4,0200, 6,6400, 6,9000, 7,0800, 8,0800, 9,0000, 9,9600,

9,9600, 10,8400, 11,7200, 12,1400, 12,3800, 12,9800, 13,3000, 13,5200, 14,9000, 15,0600, 15,2400 and 21,4000 degrees  $\theta$ .

5 33. Polymeric form I of idazoxan wherein the X-Ray spectra comprises specific peaks at about 4,0200, 6.6400, 6.9000, 7.0800, 8.0800, 9.0000, 9.9600, 9.9600, 10.8400, 11.7200, 12.1400, 12.3800, 12.9800, 13.3000, 13.5200, 14.9000, 15.0600, 15.2400 and 21.4000 degrees  
10  $\theta$  and lacking at least one peak at about 4.0200, 6.6400, 6.9000, 7.0800, 8.0800, 9.0000, 9.9600, 9.9600, 10.8400, 11.7200, 12.1400, 12.3800, 12.9800, 13.3000, 13.5200, 14.9000, 15.0600, 15.2400 and 21.4000 degrees  
15  $\theta$ .

34. Polymeric form I of idazoxan wherein the differential thermal analysis thermogram exhibiting a single maximum value at approximately  $207.5 \pm 0.2$ .

20 35. Polymeric form II of idazoxan wherein the X-Ray spectra comprises the specific peaks at about 4.7400, 5.7200, 6.6800, 7.5000, 8.9200, 9.9600, 11.5200, 12.3000, 12.9400, 13.5400, 14.3000, 15.6800, 16.8600 and 18.9000 degrees  $\theta$ .

25 36. Polymeric form II of idaxozan wherein the differential thermal analysis thermogram exhibiting a single maximum value at approximately  $203.0 \pm 0.4$ .

30 37. Polymeric form III of idazoxan wherein the X-Ray spectra comprises the specific peaks at about 4,0400, 4.7000, 5.7400, 6.6200, 6.9200, 7.4600, 8.0400, 8.7800, 8.9800, 9.9800, 10.8200, 11.4600, 11.6400, 12.3200, 12.9400, 13.5400, 14.2400, 15.0600, 15.6200 and 16.8400  
35 degrees  $\theta$ .

38. Polymeric form III of idazoxan wherein the differential thermal analysis thermogram exhibiting a single maximum value at approximately  $203.8 \pm 0.5$ .

39. Polymeric form IV of idazoxan wherein the X-Ray spectra comprises the specific peaks at about 4.8000, 5.9000, 6.8400, 7.3200, 8.0800, 8.6600, 9.4600, 9.6800, 11.1600, 11.4000, 11.9000, 12.2200, 12.6800, 13.8400, 14.4200, 14.9800 and 18.1000 degrees  $\theta$ .
40. Polymeric form IV of idazoxan wherein the X-Ray spectra comprises the specific peaks at about 4.8000, 5.9000, 6.8400, 7.3200, 8.0800, 8.6600, 9.4600, 9.6800, 11.1600, 11.4000, 11.9000, 12.2200, 12.6800, 13.8400, 14.4200, 14.9800 and 18.1000 degrees  $\theta$  and lacking at least one peak at about 6.6800, 13.5400, 15.6800, 16.8600 or 18.9000 degrees  $\theta$ .
41. Polymeric form IV of idazoxan wherein the differential thermal analysis thermogram exhibiting a single maximum value at approximately  $205.3 \pm 0.5$ .
42. Polymeric form V of idazoxan wherein the X-Ray spectra comprises the specific peaks at about 5.0400, 5.8400, 7.9400, 9.2800, 9.4400, 10.1200, 12.0200, 12.5600, 12.9200, 13.7400, 13.9400, 14.5200, 14.8200, 15.2800, 16.2800 and 16.7400 degrees  $\theta$ .
43. Polymeric form V of idazoxan wherein the X-Ray spectra comprises the specific peaks at about 5.0400, 5.8400, 7.9400, 9.2800, 9.4400, 10.1200, 12.0200, 12.5600, 12.9200, 13.7400, 13.9400, 14.5200, 14.8200, 15.2800, 16.2800 and 16.7400 degrees  $\theta$  and lacking at least one peak at about 4.7400, 6.6800, 7.5000, 8.9200, 11.5200, 14.3000, 15.6800 or 18.9000 degrees  $\theta$ .